

(FILE 'HOME' ENTERED AT 15:05:16 ON 19 AUG 2003)

FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE, CANCERLIT' ENTERED AT 15:05:27 ON  
19 AUG 2003

L1	57645 DENDRITIC CELL
L2	71976 DENDRITE
L3	28736 NUCLEAR FACTOR KAPPA B
L4	1525 NFKB
L5	55636 NF KAPPA B
L6	323 L1 AND L3
L7	9 L1 AND L4
L8	807 L1 AND L5
L9	9 DUP REM L7 (0 DUPLICATES REMOVED)
L10	6 L2 AND L3
L11	1 L2 AND L4
L12	18 L2 AND L5
L13	5 DUP REM L10 (1 DUPLICATE REMOVED)
L14	10 DUP REM L12 (8 DUPLICATES REMOVED)
L15	270 BONE MARROW-DERIVED DCS
L16	1 L15 AND L3
L17	0 L15 AND L4
L18	5 L15 AND L5
L19	2 DUP REM L18 (3 DUPLICATES REMOVED)
L20	751 DENDRITIC CELL MATURATION
L21	26 L20 AND L3
L22	0 L20 AND L4
L23	53 L20 AND L5
L24	20 DUP REM L21 (6 DUPLICATES REMOVED)

L24 ANSWER 1 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 2

ACCESSION NUMBER: 2003:113398 BIOSIS  
DOCUMENT NUMBER: PREV200300113398  
TITLE: TIRAP: An adapter molecule in the Toll signaling pathway.  
AUTHOR(S): Horng, Tiffany; Barton, Gregory M.; Medzhitov, Ruslan (1)  
CORPORATE SOURCE: (1) Howard Hughes Medical Institute, Section of  
Immunobiology, Yale University School of Medicine, New  
Haven, CT, 06520, USA: ruslan@yale.edu USA  
SOURCE: Nature Immunology, (September 2001, 2001) Vol. 2, No. 9,  
pp. 835-841. print.  
ISSN: 1529-2908.  
DOCUMENT TYPE: Article  
LANGUAGE: English

AB Mammalian Toll-like receptors (TLRs) recognize conserved products of  
microbial metabolism and activate NF-kappaB and other signaling pathways  
through the adapter protein MyD88. Although some cellular responses are  
completely abolished in MyD88-deficient mice, TLR4, but not TLR9, can  
activate NF-kappaB and mitogen-activated protein kinases and induce  
**dendritic cell maturation** in the absence of  
MyD88. These differences suggest that another adapter must exist that can  
mediate MyD88-independent signaling in response to TLR4 ligation. We have  
identified and characterized a Toll-interleukin 1 receptor (TIR)  
domain-containing adapter protein (TIRAP) and have shown that it controls  
activation of MyD88-independent signaling pathways downstream of TLR4. We  
have also shown that the double-stranded RNA-binding protein kinase PKR is  
a component of both the TIRAP- and MyD88-dependent signaling pathways.

L24 ANSWER 2 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 3

ACCESSION NUMBER: 2000:83731 BIOSIS  
DOCUMENT NUMBER: PREV200000083731  
TITLE: Dexamethasone inhibits **dendritic cell  
maturation** by redirecting differentiation of a  
subset of cells.  
AUTHOR(S): Matasic, Richard; Dietz, Allan B.; Vuk-Pavlovic, Stanimir  
(1)  
CORPORATE SOURCE: (1) Mayo Clinic, Guggenheim 1311A, Rochester, MN, 55905 USA  
SOURCE: Journal of Leukocyte Biology, (Dec., 1999) Vol. 66, No. 6,  
pp. 909-914.  
ISSN: 0741-5400.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB To investigate how corticosteroids affect differentiation of human  
dendritic cells (DC) in a defined inflammatory environment, we incubated  
immature DC with dexamethasone in the presence of tumor necrosis factor  
alpha (TNF-alpha), interleukin-1beta (IL-1beta), and prostaglandin E2.  
Dexamethasone inhibited differentiation into mature DC, as indicated by  
the reduced expression of antigen-presenting molecules, costimulatory and  
adhesion molecules, a marker of mature DC, and IL-12. Dexamethasone  
increased expression of CD14, CD36, and CD68, molecules characteristic of  
monocytes/macrophages and induced CD14+CD83- cells, a subset distinct both  
from immature DC and mature DC. The effects were concentration-dependent,  
with ID50 values between 2 and 30 nM dexamethasone. Unlike T and B cells,  
in DC dexamethasone induced no apoptosis, although it suppressed activated  
nuclear transcription factor NF-kappaB. Dexamethasone reduced the ability  
of DC to stimulate proliferation of allogeneic T cells in proportion to  
the level of CD14+CD83- cells in the population. CD83+ cells, isolated  
from dexamethasone-treated populations, retained the synthesis of IL-12  
and the ability to stimulate proliferation of allogeneic T cells. Our data  
demonstrate that the dominant effect of the drug was redirecting  
differentiation of a subset of cells despite the presence of inflammatory  
cytokines. The observed ID50 values indicate that inhibition of DC

differentiation might contribute significantly to in vivo immunosuppression by chronic administration of corticosteroids.

L24 ANSWER 3 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 2003:174585 BIOSIS  
DOCUMENT NUMBER: PREV200300174585  
TITLE: Distinct contributions of different CD40 TRAF binding sites to CD154-induced **dendritic cell maturation** and IL-12 secretion.  
AUTHOR(S): Mackey, Matthew F.; Wang, Ze; Eichelberg, Katrin; Germain, Ronald N. (1)  
CORPORATE SOURCE: (1) National Institutes of Health, 10 Center Drive, Bldg. 10, Rm. 11N311, MSC-1892, Bethesda, MD, 20892-1892, USA: matthew.mackey@aventis.com, rgermain@nih.gov USA  
SOURCE: European Journal of Immunology, (March 2003, 2003) Vol. 33, No. 3, pp. 779-789. print.  
ISSN: 0014-2980.  
DOCUMENT TYPE: Article  
LANGUAGE: English

AB The mechanisms by which CD40 controls the maturation and antigen presentation functions of dendritic cells (DC) remains largely undefined in this critical cell type. To examine this question, we have employed retroviral transduction of primary bone marrow-derived mouse DC. Mutation of the distinct binding sites for TNF receptor-associated factor 6 (TRAF6) and for TRAF 2, 3, and 5 in the CD40 cytoplasmic domain revealed their independent contributions to DC maturation and activation of NF-kappaB. In contrast, disruption of the TRAF6 but not the TRAF 2,3,5 binding site markedly decreased IL-12 p40 secretion along with p38 and JNK activation in response to CD154 stimulation. These data document a clear bifurcation of the CD40 signaling cascade in primary DC at the level of the receptor's two distinct and autonomous TRAF binding sites, and reveal the predominant role of the TRAF6 binding site in CD40-induced pro-inflammatory cytokine production by these cells.

L24 ANSWER 4 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 2002:602273 BIOSIS  
DOCUMENT NUMBER: PREV200200602273  
TITLE: Endogenous ligands of Toll-like receptors: Implications for regulating inflammatory and immune responses.  
AUTHOR(S): Beg, Amer A. (1)  
CORPORATE SOURCE: (1) Dept of Biological Sciences, Columbia University, 1212 Amsterdam Ave, 1110 Fairchild Center, New York, NY, 10027: aab41@columbia.edu USA  
SOURCE: Trends in Immunology, (November, 2002) Vol. 23, No. 11, pp. 509-512. <http://journals.bmn.com/journals/list/latest?jcode=it>. print.  
ISSN: 1471-4906.  
DOCUMENT TYPE: General Review  
LANGUAGE: English

AB Toll-like receptors (TLRs) have a crucial role in regulating immunity against microbial agents. Recent studies indicate that these receptors might also have an important role in regulating responses to endogenous stimuli, such as necrotic cells, heat-shock proteins and extracellular matrix breakdown products. Specifically, TLR2 and TLR4 were shown to mediate expression of inflammatory genes and trigger **dendritic-cell 'maturation'** by these agents. These intriguing findings suggest that the ancient family of TLRs are involved in the recognition, not only of microbes, but also of endogenous harmful stimuli. However, potential complications associated with microbial contamination of endogenous agents and the specific nature of in vivo responses induced by these agents remain to be determined.

L24 ANSWER 5 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 2002:379888 BIOSIS

DOCUMENT NUMBER: PREV200200379888  
TITLE: Measurement of **nuclear factor-kappa B** translocation on lipopolysaccharide-activated human dendritic cells by confocal microscopy and flow cytometry.  
AUTHOR(S): Blaecke, Aline; Delneste, Yves; Herbault, Nathalie; Jeannin, Pascale; Bonnefoy, Jean-Yves; Beck, Alain; Aubry, Jean-Pierre (1)  
CORPORATE SOURCE: (1) Department of Physico-Chemistry, Centre d'Immunologie Pierre Fabre, 5 Av Napoleon III, 74160, Saint Julien en Genevois: jean.pierre.aubry@pierre-fabre.com France  
SOURCE: Cytometry, (June 1, 2002) Vol. 48, No. 2, pp. 71-79.  
<http://www.interscience.wiley.com/jpages/0196-4763/>. print.  
ISSN: 0196-4763.  
DOCUMENT TYPE: Article  
LANGUAGE: English

AB Background: **Nuclear factor kappa B** (NF-kappaB) is a ubiquitously expressed transcription factor that regulates cytokine and immunoglobulin (Ig) gene expression. In most cell types, the inactive p50/p65 NF-kappaB heterodimer is located in the cytoplasm, complexed to its IkappaB inhibitory unit. Stimulation of cells by various reagents such as bacterial endotoxin or cytokines leads to a dissociation of NF-kappaB from IkappaB and a rapid translocation of free NF-kappaB to the nucleus. The aim of this article is to define optimal conditions for the measurement of NF-kappaB translocation by both confocal microscopy and flow cytometry. Methods: Four commercial anti-NF-kappaB antibodies were evaluated by confocal microscopy, after using two methods of fixation and permeabilization of the cells. These antibodies were examined further by flow cytometry on purified nuclei. Results: Paraformaldehyde-methanol treatment of dendritic cells is a good combination to visualize NF-kappaB translocation by confocal microscopy. Three of the four antibodies tested gave good results on nonactivated and on lipopolysaccharide (LPS)-activated dendritic cells. The measurement of NF-kappaB translocation by flow cytometry on purified nuclei is a quick and sensitive method. Only one of the four evaluated antibodies showed a significant difference between nonactivated and activated cells. Conclusions: Microscopy and flow cytometry are quick and reproducible methods to measure NF-kappaB translocation and can be adapted to identify new molecules that activate dendritic cells.

L24 ANSWER 6 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:442082 BIOSIS  
DOCUMENT NUMBER: PREV200100442082  
TITLE: Maturation of human dendritic cells as sulfasalazine target.  
AUTHOR(S): Matasic, Richard; Dietz, Allan B.; Vuk-Pavlovic, Stanimir (1)  
CORPORATE SOURCE: (1) Mayo Clinic, Rochester, MN, 55905: vuk\_pavlovic@mayo.edu USA  
SOURCE: Croatian Medical Journal, (August, 2001) Vol. 42, No. 4, pp. 440-445. print.  
ISSN: 0353-9504.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Aim. Sulfasalazine, a nonsteroidal anti-inflammatory drug, is effective in treating some autoimmune diseases, but its mechanism of action is unclear. To determine whether dendritic cells could be a possible target of the drug, we studied the effects of sulfasalazine and its metabolites, aminosalicylate and sulfapyridine, on in vitro maturation (terminal differentiation) of human myeloid dendritic cells. Methods. We prepared immature dendritic cells by incubating CD14-positive cells in the presence of granulocyte-macrophage colony-stimulating factor and interleukin (IL)-4. The cells were matured by addition of tumor necrosis factor

(TNF)- $\alpha$ , IL-1 $\beta$ , and prostaglandin E2 in the presence of sulfasalazine or its metabolites - aminosalicylate and sulfapyridine, or their combinations. We quantified the effect of drugs on the dendritic cell characteristics, such as stimulation of autologous and allogeneic pan-T cell proliferation, surface marker phenotype, IL-12 p40 subunit secretion, and activation of nuclear transcription factor (NF)- $\kappa$ B. Results. Dendritic cells treated with sulfasalazine (1.25  $\mu$ mol/L or 2.5  $\mu$ mol/L) could not stimulate T cells ( $p < 0.028$ , two-sided paired t-test). In distinction to drug-free maturing dendritic cells, 2.5  $\mu$ mol/L sulfasalazine upregulated the levels of CD14 and CD68 and downregulated the levels of CD40, CD80, and CD83 (for all CD markers,  $p < 0.03$  for difference between measurements in the absence and the presence of sulfasalazine). From concentration-dependent changes in CD83 expression, we found an apparent ID50 approx 1.5  $\mu$ mol/L sulfasalazine. The apparent ID50 value for aminosalicylate-inhibited maturation was 4  $\mu$ mol/L. Sulfapyridine had no effect. At 1.25  $\mu$ mol/L, sulfasalazine largely inhibited NF- $\kappa$ B activation in dendritic cells. Conclusion. Maturing human dendritic cells are hundred-fold more sensitive to sulfasalazine than T cells and NK cells and the most sensitive human cells described so far. Thus, **dendritic cell maturation** is an important target of sulfasalazine. Because of the role of dendritic cells in (auto)immunity, inhibition of their maturation might provide a target for further optimization of sulfasalazine therapy.

L24 ANSWER 7 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 ACCESSION NUMBER: 2001:322087 BIOSIS  
 DOCUMENT NUMBER: PREV200100322087  
 TITLE: Expression of different NF $\kappa$ B pathway genes in dendritic cells (DCs) or macrophages assessed by gene expression profiling.  
 AUTHOR(S): Baltathakis, Ioannis (1); Alcantara, Orlando (1); Boldt, David H. (1)  
 CORPORATE SOURCE: (1) Medicine/Hematology, University of Texas Health Science Center, San Antonio, TX USA  
 SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 611a. print.  
 Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology  
 . ISSN: 0006-4971.  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 AB NF $\kappa$ B/Rel transcription factors (mainly c-Rel, RelB, and p50) have been implicated in the differentiation of monocytes to either DCs or macrophages, as well as in the maturation of DCs from antigen-processing to antigen-presenting cells. Recent studies of the expression pattern of Rel proteins and their inhibitors (IkappaBs) suggest that their regulation during this differentiation process is transcriptional. To investigate differential gene expression between macrophages and DCs, we used commercially available gene microarrays (GEArray<sup>TM</sup> KIT), which included 4 of the NF $\kappa$ B/Rel family genes (p50/p105, p52/p100, RelB, and c-Rel) and 32 additional genes that are known to be under transcriptional control of NF $\kappa$ B/Rel factors. To generate macrophages and DCs, human adherent peripheral blood monocytes were cultured with M-CSF or GM-CSF + IL-4 respectively for 7 days. DCs (and in some experiments, macrophages) were treated with lipopolysaccharide (LPS) for the last 24 hours of culture to induce maturation. Cells were harvested after 7 days, cDNA was prepared and radiolabeled with alpha-32P-dCTP, then hybridized to gene arrays containing specific gene probes. beta-actin and GAPDH or PUC18 oligonucleotides served as positive or negative controls, respectively. The expression of all 4 NF $\kappa$ B/Rel family genes examined was significantly up-regulated in maturing DCs compared to macrophages. The strongest difference was observed for c-Rel. Sequential RT-PCR

determinations of c-Rel, RelB, and p105 mRNAs confirmed these observations. Stimulation of macrophages with LPS resulted in induction of the same genes, but the expression of c-Rel remained higher in DCs. Among the 32 NFkappa-B/Rel target genes, 11 were consistently up-regulated in mature DCs compared to macrophages. These genes were-IkappaBalpha, NIK (serine/threonine protein kinase), ICAM-1, P-selectin, TNFR2, TNFAIP3 (tumor necrosis factor alpha-induced protein), IL-1alpha, IL-1R1, IL-1R2, IRAK (IL-1 receptor-associated kinase), and TANK (TRAF family member-associated NFkappa-B activator). By contrast, only mcp-1 (monocyte chemotactic protein 1) was induced exclusively in macrophages. Results were reproducible in 2-4 independent experiments. Genes whose expression did not differ between the two types of cells included c-myc, VCAM-1, G-CSF, GM-CSF, IL-2, IL-6, and IL-8. We conclude that NFkappa-B/Rel family genes, especially c-Rel, are selectively induced during **dendritic cell maturation**. Moreover, this process is associated with expression of a unique subset of genes that are transcriptionally targeted by NFkappa-B/Rel factors.

L24 ANSWER 8 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 ACCESSION NUMBER: 2000:88966 BIOSIS  
 DOCUMENT NUMBER: PREV200000088966  
 TITLE: Differential expression of Rel/NF-kappaB and octamer factors is a hallmark of the generation and maturation of dendritic cells.  
 AUTHOR(S): Neumann, M. (1); Fries, H.-W.; Scheicher, C.; Keikavoussi, P.; Kolb-Maeurer, A.; Broecker, E.-B.; Serfling, E.; Kaempgen, E.  
 CORPORATE SOURCE: (1) Department of Molecular Pathology, Institute of Pathology, University of Wuerzburg, Josef-Schneider-Strasse 2, D-97080, Wuerzburg Germany  
 SOURCE: Blood, (Jan. 1, 2000) Vol. 95, No. 1, pp. 277-285.  
 ISSN: 0006-4971.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB A key feature of maturation of dendritic cells is the down-regulation of antigen-processing and up-regulation of immunostimulatory capacities. To study the differential expression of transcription factors in this process, we investigated the nuclear translocation and DNA binding of Rel/NF-kappaB and octamer factors during in vitro generation and maturation of dendritic cells compared with macrophage development. RelB was the only factor strongly up-regulated during the generation of both immature dendritic cells and macrophages. Cytokine-induced maturation of dendritic cells resulted in an increase in nuclear RelB, p50, p52, and especially c-Rel, whereas cytokine-treated macrophages responded poorly. This up-regulation of NF-kappaB factors did not correlate with lower levels of cytosolic NF-kappaB inhibitors, the IkappaBs. One IkappaB, Bcl-3, was strongly expressed only in mature dendritic cells. Furthermore, generation and maturation of dendritic cells led to a continuous down-regulation of the octamer factor Oct-2, whereas monocytes and macrophages displayed high Oct-2 levels. A similar pattern of maturation-induced changes in transcription factor levels was found in cultured murine epidermal Langerhans cells, suggesting a general physiological significance of these findings. Finally, this pattern of differential activation of Rel and octamer factors appears to be suitable in determining the maturation stage of dendritic cells generated by treatment with different cytokine combinations in vitro.

L24 ANSWER 9 OF 20 MEDLINE on STN DUPLICATE 4  
 ACCESSION NUMBER: 1998230465 MEDLINE  
 DOCUMENT NUMBER: 98230465 PubMed ID: 9570538  
 TITLE: Vascular endothelial growth factor affects **dendritic cell maturation** through the inhibition of **nuclear factor**

-**kappa B** activation in hemopoietic progenitor cells.

AUTHOR: Oyama T; Ran S; Ishida T; Nadaf S; Kerr L; Carbone D P; Gabrilovich D I

CORPORATE SOURCE: The Vanderbilt Cancer Center, Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN 37232, USA.

CONTRACT NUMBER: CA61242 (NCI)

SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Feb 1) 160 (3) 1224-32.  
Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199805

ENTRY DATE: Entered STN: 19980520

Last Updated on STN: 20020919

Entered Medline: 19980514

AB Vascular endothelial growth factor (VEGF), produced by almost all tumor cells, affects the ability of hemopoietic progenitor cells (HPC) to differentiate into functional dendritic cells (DC) during the early stages of their maturation. In this study we demonstrate specific binding of VEGF to HPC. This binding was efficiently competed by placenta growth factor (PIGF), a ligand reportedly specific for the Flt-1 receptor. The number of binding sites for VEGF decreased during DC maturation in vitro associated with decreased levels of mRNA for Flt-1. VEGF significantly inhibited **nuclear factor-kappa B** (NF-kappa B)-dependent activation of reporter gene transcription during the first 24 h in culture. The presence of VEGF significantly decreased the specific DNA binding of NF-kappa B as early as 30 min after induction with TNF-alpha. This was followed on days 7 to 10 by decreases in the mRNA for RelB and c-Rel, two subunits of NF-kappa B. Blockade of NF-kappa B activity in HPC at early stages of differentiation with an adenovirus expressing a dominant I kappa B inhibitor of NF-kappa B reproduced the pattern of effects observed with VEGF. Thus, NF-kappa B plays an important role in maturation of HPCs to DC, and VEGF activation of the Flt-1 receptor is able to block the activation of NF-kappa B in this system. Blockade of NF-kappa B activation in HPCs by tumor-derived factors may therefore be a mechanism by which tumor cells can directly down-modulate the ability of the immune system to generate effective antitumor immune responses.

L24 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2002:909358 CAPLUS

DOCUMENT NUMBER: 139:78717

TITLE: Immunosuppressive treatment protects against angiotensin II-induced renal damage

AUTHOR(S): Muller, Dominik N.; Shagdarsuren, Erdenechimeg; Park, Joon-Keun; Dechend, Ralf; Mervaala, Eero; Hampich, Franziska; Fiebeler, Anette; Ju, Xinsheng; Finckenberg, Piet; Theuer, Jurgen; Viedt, Christiane; Kreuzer, Joerg; Heidecke, Harald; Haller, Hermann; Zenke, Martin; Luft, Friedrich C.

CORPORATE SOURCE: HELIOS Klinikum-Berlin, Franz Volhard Clinic and Medical Faculty of the Charite, Humboldt University of Berlin, Berlin, Germany

SOURCE: American Journal of Pathology (2002), 161(5), 1679-1693

CODEN: AJPA44; ISSN: 0002-9440

PUBLISHER: American Society for Investigative Pathology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Angiotensin (Ang) II promotes renal infiltration by immunocompetent cells in double-transgenic rats (dTGrs) harboring both human renin and

angiotensinogen genes. To elucidate disease mechanisms, we investigated whether or not dexamethasone (DEXA) immunosuppression ameliorates renal damage. Untreated dTGRs developed hypertension, renal damage, and 50% mortality at 7 wk. DEXA reduced albuminuria, renal fibrosis, vascular reactive oxygen stress, and prevented mortality, independent of blood pressure. In dTGR kidneys, p22phox immunostaining co-localized with macrophages and partially with T cells. The dTGR dendritic cells expressed major histocompatibility complex II and CD86, indicating maturation. DEXA suppressed major histocompatibility complex II+, CD86+, dendritic, and T-cell infiltration. In addnl. expts., we treated dTGRs with mycophenolate mofetil to inhibit T- and B-cell proliferation. Reno-protective actions of mycophenolate mofetil and its effect on dendritic and T cells were similar to those obtained with DEXA. We next investigated whether or not Ang II directly promotes **dendritic cell maturation** in vitro. Ang II did not alter CD80, CD83, and MHC II expression, but increased CCR7 expression and cell migration. To explore the role of tumor necrosis factor (TNF)-.alpha. on **dendritic cell maturation** in vivo, we treated dTGRs with the sol. TNF-.alpha. receptor etanercept. This treatment had no effect on blood pressure, but decreased albuminuria, **nuclear factor-.kappa.B** activation, and infiltration of all immunocompetent cells. These data suggest that immunosuppression prevents **dendritic cell maturation** and T-cell infiltration in a nonimmune model of Ang II-induced renal damage. Ang II induces dendritic migration directly, whereas in vivo TNF-.alpha. is involved in dendritic cell infiltration and maturation. Thus, Ang II may initiate events leading to innate and acquired immune response.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:453103 CAPLUS  
DOCUMENT NUMBER: 139:34825  
TITLE: NF-.kappa.B in allograft rejection  
AUTHOR(S): Wei, Jian-Feng; Zheng, Shu-Sen  
CORPORATE SOURCE: Department of Hepatobiliary Surgery, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 310003, Peop. Rep. China  
SOURCE: Hepatobiliary & Pancreatic Diseases International (2003), 2(2), 180-183  
CODEN: HPDIAJ; ISSN: 1499-3872  
PUBLISHER: First Affiliated Hospital, Zhejiang University School of Medicine  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review. **Nuclear factor-kappa B** (NF-.kappa.B) as an essential transcription factor in the control of expression of the cytokine-induced genes in immune and inflammatory responses regulates cytokines in allograft rejection. In this review, the authors summarize the general properties of NF-.kappa.B and the principal findings to shed new light on transplantation.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:774920 CAPLUS  
DOCUMENT NUMBER: 136:68640  
TITLE: Bifurcation of osteoclasts and dendritic cells from common progenitors  
AUTHOR(S): Miyamoto, Takeshi; Ohneda, Osamu; Arai, Fumio; Iwamoto, Katsuya; Okada, Seiji; Takagi, Katsumasa; Anderson, Dirk M.; Suda, Toshio  
CORPORATE SOURCE: Department of Cell Differentiation, Institute of Molecular Embryology and Genetics, Kumamoto University

SOURCE: School of Medicine, Honjo, Japan  
Blood (2001), 98(8), 2544-2554  
CODEN: BLOOAW; ISSN: 0006-4971  
PUBLISHER: American Society of Hematology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Osteoclasts and dendritic cells are derived from monocyte/macrophage precursor cells; however, how their lineage commitment is regulated is unknown. This study investigated the differentiation pathways of osteoclasts and dendritic cells from common precursor cells at the single-cell level. Osteoclastogenesis induced by macrophage colony-stimulating factor (M-CSF) and receptor activator of **nuclear factor- $\kappa$ B** ligand (RANKL) or tumor necrosis factor- $\alpha$ . (TNF- $\alpha$ .) is completely inhibited by addn. of granulocyte-macrophage colony-stimulating factor (GM-CSF) or interleukin-3 at early stages of differentiation. GM-CSF-treated cells express both c-Fos and RANK and also low levels of CD11c and DEC205, which are detected on dendritic cells. Addn. of GM-CSF also reduces expression of both c-Fos and Fra-1, which is an important event for inhibition of osteoclastogenesis. Overexpression of c-Fos by retroviral infection or induction in transgenic mice can rescue a failure in osteoclast differentiation even in the presence of GM-CSF. By contrast, differentiation into dendritic cells is inhibited by M-CSF, indicating that M-CSF and GM-CSF reciprocally regulate the differentiation of both lineages. **Dendritic cell maturation** is also inhibited when c-Fos is expressed at an early stage of differentiation. Taken together, these findings suggest that c-Fos is a key mediator of the lineage commitment between osteoclasts and dendritic cells. The lineage detn. of osteoclast progenitors seen following GM-CSF treatment functions through the regulation of c-Fos expression.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:775102 CAPLUS

DOCUMENT NUMBER: 136:84459

TITLE: A DAP12-mediated pathway regulates expression of CC chemokine receptor 7 and maturation of human dendritic cells

AUTHOR(S): Bouchon, Axel; Hernandez-Munain, Cristina; Cella, Marina; Colonna, Marco

CORPORATE SOURCE: Basel Institute for Immunology, Basel, CH-4005, Switz.

SOURCE: Journal of Experimental Medicine (2001), 194(8), 1111-1122

CODEN: JEMEAV; ISSN: 0022-1007

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Gene targeting of the adaptor mol. DAP12 in mice caused abnormal distribution and impaired antigen presentation capacity of dendritic cells (DCs). However, the DAP12-assocd. receptors expressed on DCs and their functions have not been identified yet. Here we show that the triggering receptor expressed on myeloid cells-2 (TREM-2) is a cell surface receptor on human monocyte-derived DCs, which is assocd. with DAP12. TREM-2/DAP12 promotes upregulation of CC chemokine receptor 7, partial DC maturation, and DC survival through activation of protein tyrosine kinases and extracellular signal-regulated kinase. In contrast to Toll-like receptor-mediated signaling, TREM2/DAP12 stimulation is independent of **nuclear factor- $\kappa$ B** and p38 stress-activated protein kinase. This novel DC activation pathway may regulate DC homeostasis and amplify DC responses to pathogens, explaining the phenotype obsd. in DAP12-deficient mice.

REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN  
 ACCESSION NUMBER: 2000:741911 CAPLUS  
 DOCUMENT NUMBER: 133:308991  
 TITLE: Compositions containing immunotoxins and agents that inhibit **dendritic cell maturation** for inducing immune tolerance to a graft  
 INVENTOR(S): Neville, David M.; Thomas, Judith M.  
 PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; UAB Research Foundation  
 SOURCE: PCT Int. Appl., 34 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061132	A1	20001019	WO 2000-US10253	20000414
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000043542	A5	20001114	AU 2000-43542	20000414
BR 2000009772	A	20020108	BR 2000-9772	20000414
EP 1171109	A1	20020116	EP 2000-923415	20000414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541195	T2	20021203	JP 2000-610465	20000414
PRIORITY APPLN. INFO.:				
			US 1999-291712	A2 19990414
			WO 2000-US10253	W 20000414
AB The present invention provides a method of inducing immune tolerance to a graft in a recipient, comprising administering to the recipient an immunotoxin, thereby reducing the recipient's T-cell population; and administering to the recipient an agent that inhibits <b>dendritic cell maturation</b> . The present invention also provides a method of screening for an agent that acts synergistically with an immunotoxin in inducing immune tolerance and a method of screening for an agent that inhibits <b>dendritic cell maturation</b> . . The present invention also provides a method of treating a subject with an autoimmune disease, comprising administering to the subject an immunotoxin, thereby reducing the subject's T-cell population; and administering to the subject an agent that inhibits <b>dendritic cell maturation</b> . Also provided herein is a compn. comprising an immunotoxin and an agent that inhibits <b>dendritic cell maturation</b> .				
REFERENCE COUNT:	9	THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L24 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN  
 ACCESSION NUMBER: 2000:722609 CAPLUS  
 DOCUMENT NUMBER: 133:361898  
 TITLE: Recombinant adenovirus induces maturation of dendritic cells via an NF- $\kappa$ B-dependent pathway  
 AUTHOR(S): Morelli, Adrian E.; Larregina, Adriana T.; Ganster, Raymond W.; Zahorchak, Alan F.; Plowey, Jeffrey M.; Takayama, Takuya; Logar, Alison J.; Robbins, Paul D.;

CORPORATE SOURCE: Faló, Louis D.; Thomson, Angus W.  
Thomas E. Starzl Transplantation Institute, Department  
of Surgery, University of Pittsburgh Medical Center,  
Pittsburgh, PA, 15213-2582, USA  
SOURCE: Journal of Virology (2000), 74(20), 9617-9628  
CODEN: JOVIAM; ISSN: 0022-538X  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Recombinant adenovirus (rAd) infection is one of the most effective and frequently employed methods to transduce dendritic cells (DC). Contradictory results have been reported recently concerning the influence of rAd on the differentiation and activation of DC. In this report, we show that, as a result of rAd infection, mouse bone marrow-derived immature DC upregulate expression of major histocompatibility complex class I and II antigens, costimulatory mol. (CD40, CD80, and CD86), and the adhesion mol. CD54 (ICAM-1). rAd-transduced DC exhibited increased allostimulatory capacity and levels of interleukin-6 (IL-6), IL-12p40, IL-15, gamma interferon, and tumor necrosis factor alpha mRNAs, without effects on other immunoregulatory cytokine transcripts such as IL-10 or IL-12p35. These effects were not related to specific transgenic sequences or to rAd genome transcription. The rAd effect correlated with a rapid increase (1 h) in the NF- $\kappa$ B-DNA binding activity detected by electrophoretic mobility shift assays. rAd-induced DC maturation was blocked by the proteasome inhibitor N.alpha.-p-tosyl-L-lysine chloromethyl ketone (TLCK) or by infection with rAd-I. $\kappa$ B, an rAd-encoding the dominant-neg. form of I. $\kappa$ B. In vivo studies showed that after i.v. administration, rAds were rapidly entrapped in the spleen by marginal zone DC that mobilized to T-cell areas, a phenomenon suggesting that rAd also induced DC differentiation in vivo. These findings may explain the immunogenicity of rAd and the difficulties in inducing long-term antigen-specific T-cell hyporesponsiveness with rAd-transduced DC.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:771388 CAPLUS

DOCUMENT NUMBER: 134:41044

TITLE: Maturation-dependent expression and function of the CD49d integrin on monocyte-derived human dendritic cells

AUTHOR(S): Puig-Kroger, Amaya; Sanz-Rodriguez, Francisco; Longo, Natividad; Sanchez-Mateos, Paloma; Botella, Luisa; Teixido, Joaquin; Bernabeu, Carmelo; Corbi, Angel L.

CORPORATE SOURCE: Centro de Investigaciones Biologicas, Consejo Superior de Investigaciones Cientificas, Madrid, 28006, Spain

SOURCE: Journal of Immunology (2000), 165(8), 4338-4345

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Dendritic cells (DC) are highly specialized APC that are crit. for the initiation of T cell-dependent immune responses. DC exert a sentinel function while immature and, after activation by inflammatory stimuli or infectious agents, mature and migrate into lymphoid organs to prime T cells. The authors have analyzed integrin expression on monocyte-derived DC (MDDC) and found that expression of CD49d integrins (CD49d/CD29 and CD49d/.beta.7) was induced/up-regulated during TNF-.alpha.- or LPS-initiated MDDC maturation, reflecting the induction/up-regulation of CD49d and .beta.7 mRNA. CD49d mRNA steady-state level increased more than 10 times during maturation, with the highest levels obsd. 24 h after TNF-.alpha. treatment. CD49d integrin expression conferred mature MDDC with an elevated capacity to adhere to the CS-1 fragment of fibronectin, and also mediated transendothelial migration of mature MDDC.

Up-regulation of CD49d integrin expression closely paralleled that of the mature DC marker CD83. CD49d integrin expression was dependent on cell maturation, as its induction was abrogated by N-acetylcysteine, which inhibits NF- $\kappa$ B activation and the functional and phenotypic maturation of MDDC. Moreover, CD49d integrin up-regulation and MDDC maturation were prevented by SB 203580, a specific inhibitor of p38 mitogen-activated protein kinase, but were almost unaffected by the mitogen-activated protein/extracellular signal-related kinase kinase 1/2 inhibitor PD 98059. Our results support the existence of a link between functional and phenotypic maturation of MDDC and CD49d integrin expression, thus establishing CD49d as a maturation marker for MDDC. The differential expression of CD49d on immature and mature MDDC might contribute to their distinct motility capabilities and mediate mature DC migration into lymphoid organs.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:904923 CAPLUS

DOCUMENT NUMBER: 134:161862

TITLE: A Toll-like receptor recognizes bacterial DNA

AUTHOR(S): Hemmi, Hiroaki; Takeuchi, Osamu; Kawai, Taro; Kaisho, Tsuneyasu; Sato, Shintaro; Sanjo, Hideki; Matsumoto, Makoto; Hoshino, Katsuaki; Wagner, Hermann; Takeda, Kiyoshi; Akira, Shizuo

CORPORATE SOURCE: Department of Host Defense, Research Institute for Microbial Diseases, Osaka University and Core Research for Evolutional Science and Technology, Suita, Osaka, 565-0871, Japan

SOURCE: Nature (London) (2000), 408(6813), 740-745

CODEN: NATUAS; ISSN: 0028-0836

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB DNA from bacteria has stimulatory effects on mammalian immune cells, which depend on the presence of unmethylated CpG dinucleotides in the bacterial DNA. In contrast, mammalian DNA has a low frequency of CpG dinucleotides, and these are mostly methylated; therefore, mammalian DNA does not have immuno-stimulatory activity. CpG DNA induces a strong T-helper-1-like inflammatory response. Accumulating evidence has revealed the therapeutic potential of CpG DNA as adjuvants for vaccination strategies for cancer, allergy and infectious diseases. Despite its promising clin. use, the mol. mechanism by which CpG DNA activates immune cells remains unclear. Here the authors show that cellular response to CpG DNA is mediated by a Toll-like receptor, TLR9. TLR9-deficient (TLR9<sup>-/-</sup>) mice did not show any response to CpG DNA, including proliferation of splenocytes, inflammatory cytokine prodn. from macrophages and maturation of dendritic cells. TLR9<sup>-/-</sup> mice showed resistance to the lethal effect of CpG DNA without any elevation of serum pro-inflammatory cytokine levels. The in vivo CpG-DNA-mediated T-helper type-1 response was also abolished in TLR9<sup>-/-</sup> mice. Thus, vertebrate immune systems appear to have evolved a specific Toll-like receptor that distinguishes bacterial DNA from self-DNA.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:702410 CAPLUS

DOCUMENT NUMBER: 133:359008

TITLE: Cyclooxygenase-independent inhibition of **dendritic cell maturation** by aspirin

AUTHOR(S): Matasic, R.; Dietz, A. B.; Vuk-Pavlovic, S.

CORPORATE SOURCE: Stem Cell Laboratory, Mayo Clinic Cancer Center, Mayo Clinic and Mayo Foundation, Rochester, MN, 55905, USA

SOURCE: Immunology (2000), 101(1), 53-60  
CODEN: IMMUAM; ISSN: 0019-2805  
PUBLISHER: Blackwell Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB When immature human myeloid dendritic cells were differentiated in vitro in the presence of aspirin, they were unable to stimulate T-cell proliferation. Aspirin and its major metabolite salicylate changed the surface marker phenotype of dendritic cells. The drugs particularly suppressed the levels of CD83 and the secreted p40 unit of interleukin-12 (IL-12), both markers of mature dendritic cells; 50% inhibitory concn. (IC50) values were 2.5 mM, a concn. >100 times greater than the concn. at mid-point inhibition (ID50) value for inhibition of prostaglandin synthesis. Concomitantly, the levels of CD14, a marker of monocytes/macrophages, increased above the levels found in immature dendritic cells. Cyclooxygenase inhibitors ketoprofen, indomethacin, and NS-398 had no effect at concns. >1000-fold higher than their IC50 values. The effects were independent of the presence of prostaglandin E2 in the medium. Salicylates suppressed activation of the nuclear transcription factor  $\kappa$ B, which regulates dendritic cell differentiation, but their effects on mature dendritic cells were negligible. Hence, aspirin inhibits dendritic cell function by inhibiting their terminal differentiation at concns. achieved in the blood of patients chronically treated with high-dose aspirin.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:54638 CAPLUS  
DOCUMENT NUMBER: 132:346572

TITLE: Peritransplant tolerance induction in macaques: early events reflecting the unique synergy between immunotoxin and deoxyspergualin

AUTHOR(S): Thomas, Judith M.; Contreras, Juan L.; Jiang, Xiao L.; Eckhoff, Devin E.; Wang, Pei X.; Hubbard, William J.; Lobashevsky, Andrew L.; Wang, Weila; Asiedu, Clement; Stavrou, Scott; Cook, William J.; Robbin, Michelle L.; Thomas, Francis T.; Neville, David M., Jr.

CORPORATE SOURCE: Department of Surgery, Division of Transplantation Immunobiology, Departments of Pathology and Radiology, University of Alabama at Birmingham, Birmingham, AL, 35294, USA

SOURCE: Transplantation (1999), 68(11), 1660-1673  
CODEN: TRPLAU; ISSN: 0041-1337

PUBLISHER: Lippincott Williams & Wilkins  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Background. Day of transplant T cell depletion with anti-CD3 immunotoxin or F(Ab)2 immunotoxin induces stable tolerance to renal allografts in rhesus monkeys given 15-deoxyspergualin (DSG), a NF- $\kappa$ B inhibitor that suppresses proinflammatory cytokine (PC) prodn. Because PC and NF- $\kappa$ B are involved in dendritic cell (DC) maturation, we asked if impaired DC maturation and Th2-type cytokine deviation might be related to the synergistic effect of DSG in this novel model. Methods. Immunosuppression was initiated 4 h before transplanting a major histocompatibility complex mismatched renal allograft. Some groups received a supplemental 5-day course of cyclosporine A or DSG or a 15-day course of DSG. Peripheral lymph nodes were sequentially examd. for presence of mature DC. In vitro effects of DSG on PC-induced maturation of DC were also examd. Results. Allografts survived without rejection in 87% of recipients given immunotoxin or F(Ab)2 immunotoxin with DSG .times. 15 days, in 50% with DSG .times. 5 days, and 0% with cyclosporine A. The longest DSG survivors are > 1000 days with normal graft function and tolerance validated, including acceptance of challenge second donor

kidneys without treatment. DSG-treated recipients were unique in developing polarized Th2-type plasma cytokines. In DSG recipients, mature DC were significantly reduced in day +5 lymph node biopsies, with complete repopulation by 30 days. In vitro studies verified an inhibitory effect of DSG on DC maturation. Conclusions. The study suggests DSG arrests DC maturation. The unusual synergy of immunotoxin and DSG apparently involves coincidental redn. in lymph node T cell mass and mature DC, a transient circumstance favoring development of stable tolerance.

REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:797301 CAPLUS

DOCUMENT NUMBER: 130:152509

TITLE: Dendritic cell survival and maturation are regulated by different signaling pathways

AUTHOR(S): Rescigno, Maria; Martino, Manuela; Sutherland, Claire L.; Gold, Michael R.; Ricciardi-Castagnoli, Paola

CORPORATE SOURCE: Consiglio Nazionale delle Ricerche Center of Molecular and Cellular Pharmacology and the Department of Biotechnology and Biological Sciences, Second University of Milano, Milan, 20126, Italy

SOURCE: Journal of Experimental Medicine (1998), 188(11), 2175-2180

CODEN: JEMEAV; ISSN: 0022-1007

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Although dendritic cell (DC) activation is a crit. event for the induction of immune responses, the signaling pathways involved in this process have not been characterized. In this report, the authors show that DC activation induced by lipopolysaccharide (LPS) can be sepd. into two distinct processes: first, maturation, leading to upregulation of MHC and costimulatory mols., and second, rescue from immediate apoptosis after withdrawal of growth factors (survival). Using a DC culture system that allowed the authors to propagate immature growth factor-dependent DCs, the authors have investigated the signaling pathways activated by LPS. The authors found that LPS induced nuclear translocation of the nuclear factor (NF)- $\kappa$ B transcription factor. Inhibition of NF- $\kappa$ B activation blocked maturation of DCs in terms of upregulation of major histocompatibility complex and costimulatory mols. In addn., the authors found that LPS activated the extracellular signal-regulated kinase (ERK), and that specific inhibition of MEK1, the kinase which activates ERK, abrogated the ability of LPS to prevent apoptosis but did not inhibit DC maturation or NF- $\kappa$ B nuclear translocation. These results indicate that ERK and NF- $\kappa$ B regulate different aspects of LPS-induced DC activation: ERK regulates DC survival whereas NF- $\kappa$ B is responsible for DC maturation.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT